

Appl. No. 10/817,334

Prv Amdt and Resp. to Restr. Rqmt. dated March 28, 2006

Reply to Office Action of November 29, 2005

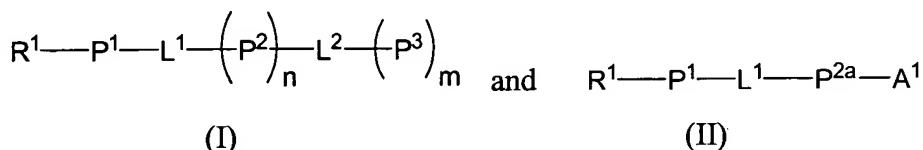
PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Withdrawn) A method for inhibiting a soluble epoxide hydrolase, comprising contacting said soluble epoxide hydrolase with an inhibiting amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5-C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;

$P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;

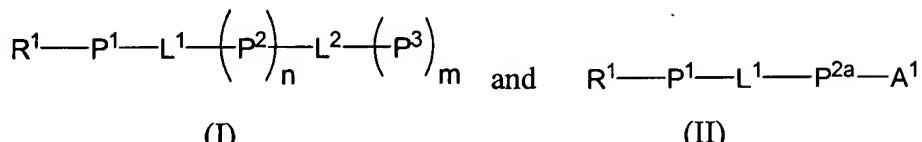
the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

2. (Withdrawn) A method for inhibiting a soluble epoxide hydrolase, comprising contacting said soluble epoxide hydrolase with an inhibiting amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5$ - $C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-O(CH_2CH_2O)_q-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;

$P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2$ - $C_6$  alkynyl,  $C_1$ - $C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1$ - $C_4$  alkyl, substituted or unsubstituted  $C_3$ - $C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1$ - $C_4$  alkyl;

the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and the subscript  $q$  is 0 to 3;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_6$  alkylene, substituted and unsubstituted  $C_3$ - $C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog

3. (Withdrawn) The method in accordance with claim 1, wherein  $R^1$  is selected from the group consisting of  $C_5$ - $C_{12}$  cycloalkyl, phenyl and naphthyl.

4. (Withdrawn) The method in accordance with claim 1, wherein  $P^1$  is selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$  and  $-NHC(O)O-$ .

5. (Withdrawn) The method in accordance with claim 1, wherein the compound has formula (I), wherein  $P^1$  is selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$  and  $-NHC(O)O-$ ;  $P^2$  is selected from the group consisting of  $-C(O)O-$ ,  $-CH(OH)-$ ,  $-OC(O)-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;  $m$  is 0 and  $L^1$  is selected from the group consisting of unsubstituted  $C_2$ - $C_6$  alkylene.

6. (Withdrawn) The method in accordance with claim 1, wherein the compound has formula (I), wherein  $P^1$  is selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$  and  $-NHC(O)O-$ ;  $P^2$  is selected from the group consisting of  $-C(O)O-$ ,  $-OC(O)-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;  $n$  and  $m$  are each 1;  $L^1$  is selected from the group consisting of unsubstituted  $C_2$ - $C_6$  alkylene;  $L^2$  is selected from the group consisting of substituted or unsubstituted  $C_2$ - $C_6$  alkylene; and  $P^3$  is selected from the group consisting of  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ , and  $-C(O)OR^2$ , wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1$ - $C_4$  alkyl, substituted or unsubstituted  $C_3$ - $C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1$ - $C_4$  alkyl.

7. (Withdrawn) The method in accordance with claim 1, wherein the compound has formula (I), wherein  $P^1$  is selected from the group consisting of  $-\text{NHC(O)NH-}$ ,  $-\text{OC(O)NH-}$  and  $-\text{NHC(O)O-}$ ;  $n$  is 0;  $m$  is 1;  $L^1$  is selected from the group consisting of unsubstituted  $C_2$ - $C_6$  alkylene;  $L^2$  is selected from the group consisting of substituted or unsubstituted  $C_2$ - $C_6$  alkylene; and  $P^3$  is selected from the group consisting of  $-\text{C(O)NHR}^2$ ,  $-\text{C(O)NHS(O)}_2\text{R}^2$ ,  $-\text{NHS(O)}_2\text{R}^2$ , and  $-\text{C(O)OR}^2$ , wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1$ - $C_4$  alkyl, substituted or unsubstituted  $C_3$ - $C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1$ - $C_4$  alkyl.

8. (Withdrawn) The method in accordance with claim 1, wherein said compound has formula (II) wherein  $A^1$  is a dipeptide or dipeptide analog.

9. (Withdrawn) The method in accordance with claim 8, wherein  $A^1$  is a dipeptide having an N-terminal residue selected from the group consisting of Tyr, His, Lys, Phe and Trp, and a C-terminal residue selected from the group consisting of Ala, Arg, Asp, Gly, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val.

10. (Withdrawn) The method in accordance with claim 1, wherein  $m$  is 1 and  $P^3$  is selected from those groups that reduce metabolism by esterase dependent inactivation, beta- oxidation, P450-dependent omega hydroxylation or by inhibiting P450 omega hydroxylase.

11. (Withdrawn) The method in accordance with claim 2, wherein  $R^1$  is selected from the group consisting of  $C_5$ - $C_{12}$  cycloalkyl, phenyl and naphthyl.

12. (Withdrawn) The method in accordance with claim 2, wherein  $P^1$  is selected from the group consisting of  $-\text{NHC(O)NH-}$ ,  $-\text{OC(O)NH-}$  and  $-\text{NHC(O)O-}$ .

13. (Withdrawn) The method in accordance with claim 2, wherein the compound has formula (I), wherein  $P^1$  is selected from the group consisting of  $-\text{NHC(O)NH-}$ ,  $-\text{OC(O)NH-}$  and  $-\text{NHC(O)O-}$ ;  $P^2$  is selected from the group consisting of  $-\text{C(O)O-}$ ,  $-\text{CH(OH)-}$ ,  $-\text{O(CH}_2\text{CH}_2\text{O)}_q\text{-}$ ,  $-\text{OC(O)-}$ ,  $-\text{C(O)NH-}$  and  $-\text{NHC(O)-}$ ;  $m$  is 0 and  $L^1$  is selected from the group consisting of unsubstituted

C<sub>2</sub>-C<sub>6</sub> alkylene, substituted and unsubstituted C<sub>3</sub>-C<sub>6</sub> cycloalkylene, and substituted or unsubstituted arylene.

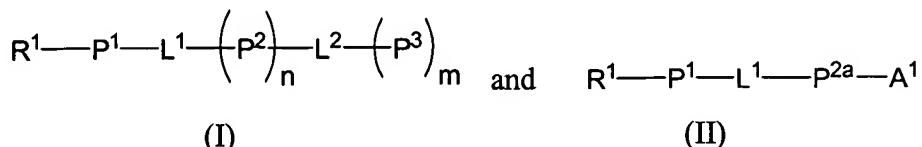
**14. (Withdrawn)** The method in accordance with claim 2, wherein the compound has formula (I), wherein P<sup>1</sup> is selected from the group consisting of -NHC(O)NH-, -OC(O)NH- and -NHC(O)O-; P<sup>2</sup> is selected from the group consisting of -C(O)O-, -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>-, -OC(O)-, -C(O)NH- and -NHC(O)-; n and m are each 1; L<sup>1</sup> is selected from the group consisting of unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene, substituted and unsubstituted C<sub>3</sub>-C<sub>6</sub> cycloalkylene, and substituted or unsubstituted arylene; L<sup>2</sup> is selected from the group consisting of substituted or unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene; and P<sup>3</sup> is selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, -NHS(O)<sub>2</sub>R<sup>2</sup>, -C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl.

**15. (Withdrawn)** The method in accordance with claim 2, wherein the compound has formula (I), wherein P<sup>1</sup> is selected from the group consisting of -NHC(O)NH-, -OC(O)NH- and -NHC(O)O-; n is 0; m is 1; L<sup>1</sup> is selected from the group consisting of unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene, substituted and unsubstituted C<sub>3</sub>-C<sub>6</sub> cycloalkylene, and substituted or unsubstituted arylene; L<sup>2</sup> is selected from the group consisting of substituted or unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene; and P<sup>3</sup> is selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, -NHS(O)<sub>2</sub>R<sup>2</sup>, -C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl.

**16. (Withdrawn)** The method in accordance with claim 2, wherein m is 1 and P<sup>3</sup> is selected from those groups that reduce metabolism by esterase dependent inactivation, beta- oxidation, P450-dependent omega hydroxylation or by inhibiting P450 omega hydroxylase.

17. (Withdrawn) A method for inhibiting a soluble epoxide hydrolase, comprising contacting said soluble epoxide hydrolase with an inhibiting amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

18. (Withdrawn) A method of treating diseases modulated by soluble epoxide hydrolases, said method comprising administering to a subject in need of such treatment an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5-C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;

$P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;

the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

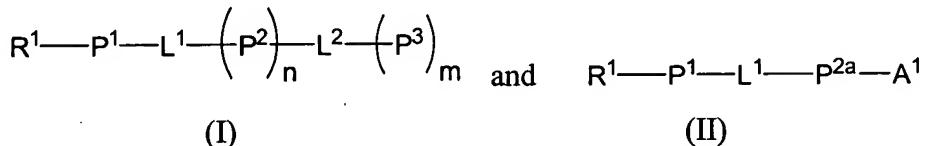
$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**19.** (Withdrawn) The method in accordance with claim 18, wherein said disease is selected from the group consisting of hypertension, inflammation, adult respiratory distress syndrome; diabetic complications; end stage renal disease; Raynaud syndrome and arthritis.

**20.** (Withdrawn) The method in accordance with claim 19, wherein said hypertension is selected from the group consisting of renal hypertension, pulmonary hypertension and hepatic hypertension.

**21.** (Withdrawn) The method in accordance with claim 19, wherein said inflammation is selected from the group consisting of renal inflammation, vascular inflammation, and lung inflammation.

**22.** (Withdrawn) A method of treating diseases modulated by soluble epoxide hydrolases, said method comprising administering to a subject in need of such treatment an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5$ - $C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-O(CH_2CH_2O)_q-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;  
 $P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)R^2$ ,  $-NHS(O)R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;  
the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and the subscript  $q$  is 0 to 3;  
 $L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted and unsubstituted  $C_3-C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;  
 $L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2-C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and  
 $A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**23.** (Withdrawn) The method in accordance with claim 22, wherein said disease is selected from the group consisting of hypertension, inflammation, adult respiratory distress syndrome; diabetic complications; end stage renal disease; Raynaud syndrome and arthritis.

**24.** (Withdrawn) The method in accordance with claim 23, wherein said hypertension is selected from the group consisting of renal hypertension, pulmonary hypertension and hepatic hypertension.

**25.** (Withdrawn) The method in accordance with claim 23, wherein said inflammation is selected from the group consisting of renal inflammation, vascular inflammation, and lung inflammation.

**26.** (Withdrawn) A method of treating diseases modulated by soluble epoxide hydrolases, said method comprising administering to a subject in need of such treatment an effective amount of a

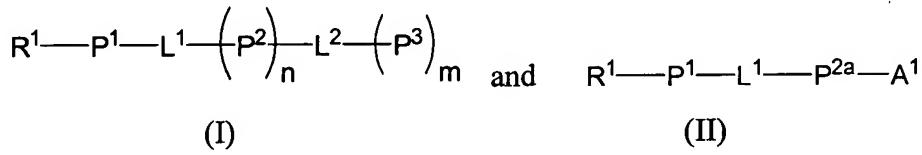
compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

**27. (Withdrawn)** The method in accordance with claim 26, wherein said disease is selected from the group consisting of hypertension, inflammation, adult respiratory distress syndrome; diabetic complications; end stage renal disease; Raynaud syndrome and arthritis.

**28. (Withdrawn)** The method in accordance with claim 27, wherein said hypertension is selected from the group consisting of renal hypertension, pulmonary hypertension and hepatic hypertension.

**29. (Withdrawn)** The method in accordance with claim 27, wherein said inflammation is selected from the group consisting of renal inflammation, vascular inflammation, and lung inflammation.

**30. (Withdrawn)** A method for reducing renal deterioration in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$\text{R}^1$  is a member selected from the group consisting of  $\text{C}_5\text{-C}_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$\text{P}^1$  is a primary pharmacophore selected from the group consisting of  $-\text{NHC}(\text{O})\text{NH}-$ ,  $-\text{OC}(\text{O})\text{NH}-$ ,  $-\text{NHC}(\text{O})\text{O}-$ ,  $-\text{CH}_2\text{C}(\text{O})\text{NH}-$ ,  $-\text{C}(\text{O})\text{NH}-$  and  $-\text{NHC}(\text{O})-$ ;

$\text{P}^2$  is a secondary pharmacophore selected from the group consisting of  $-\text{C}(\text{O})-$ ,  $-\text{CH}(\text{OH})-$ ,  $-\text{C}(\text{O})\text{O}-$ ,  $-\text{OC}(\text{O})-$ ,  $-\text{NHC}(\text{O})\text{NH}-$ ,  $-\text{OC}(\text{O})\text{NH}-$ ,  $-\text{NHC}(\text{O})\text{O}-$ ,  $-\text{C}(\text{O})\text{NH}-$  and  $-\text{NHC}(\text{O})-$ ;

$\text{P}^{2a}$  is selected from the group consisting of  $-\text{C}(\text{O})-$  and  $-\text{NHC}(\text{O})-$ ;

$\text{P}^3$  is a tertiary pharmacophore selected from the group consisting of  $\text{C}_2\text{-C}_6$  alkynyl,  $\text{C}_1\text{-C}_6$  haloalkyl, aryl, heteroaryl,  $-\text{C}(\text{O})\text{NHR}^2$ ,  $-\text{C}(\text{O})\text{NHS}(\text{O})_2\text{R}^2$ ,  $-\text{NHS}(\text{O})_2\text{R}^2$ ,

-C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl;

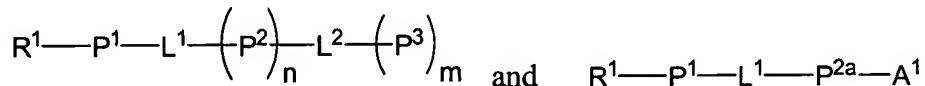
the subscripts n and m are each independently 0 or 1, and at least one of n or m is 1; L<sup>1</sup> is a first linker selected from the group consisting of substituted and unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

L<sup>2</sup> is a second linker selected from the group consisting of substituted and unsubstituted C<sub>2</sub>-C<sub>12</sub> alkylene, substituted and unsubstituted arylene, and combinations thereof; and

A<sup>1</sup> is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**31.** (Withdrawn) The method in accordance with claim 30, wherein said renal deterioration is present in said subject afflicted with diabetes, hypertension or an inflammatory disorder.

**32.** (Withdrawn) A method for reducing renal deterioration in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



(I)

(II)

and their pharmaceutically acceptable salts, wherein

R<sup>1</sup> is a member selected from the group consisting of C<sub>5</sub>-C<sub>12</sub> cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

P<sup>1</sup> is a primary pharmacophore selected from the group consisting of -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -CH<sub>2</sub>C(O)NH-, -C(O)NH- and -NHC(O)-;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  
 $-CH(OH)-$ ,  $-O(CH_2CH_2O)_q-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  
 $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;

$P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ ,  
 $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;

the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and  
the subscript  $q$  is 0 to 3;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted and unsubstituted  $C_3-C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2-C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof;  
and

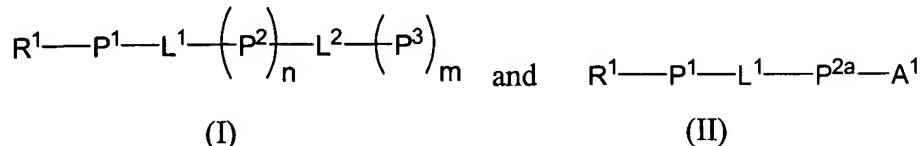
$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

33. (Withdrawn) The method in accordance with claim 32, wherein said renal deterioration is present in said subject afflicted with diabetes, hypertension or an inflammatory disorder.

34. (Withdrawn) A method for reducing renal deterioration in a subject, said method comprising administering to said subject an effective amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

35. (Withdrawn) The method in accordance with claim 34, wherein said renal deterioration is present in said subject afflicted with diabetes, hypertension or an inflammatory disorder.

36. (Withdrawn) A method for inhibiting progression of nephropathy in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$\text{R}^1$  is a member selected from the group consisting of  $\text{C}_5\text{-C}_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$\text{P}^1$  is a primary pharmacophore selected from the group consisting of  $-\text{NHC(O)NH-}$ ,  $-\text{OC(O)NH-}$ ,  $-\text{NHC(O)O-}$ ,  $-\text{CH}_2\text{C(O)NH-}$ ,  $-\text{C(O)NH-}$  and  $-\text{NHC(O)-}$ ;

$\text{P}^2$  is a secondary pharmacophore selected from the group consisting of  $-\text{C(O)-}$ ,  $-\text{CH(OH)-}$ ,  $-\text{O(CH}_2\text{CH}_2\text{O)}_q-$ ,  $-\text{C(O)O-}$ ,  $-\text{OC(O)-}$ ,  $-\text{NHC(O)NH-}$ ,  $-\text{OC(O)NH-}$ ,  $-\text{NHC(O)O-}$ ,  $-\text{C(O)NH-}$  and  $-\text{NHC(O)-}$ ;

$\text{P}^{2a}$  is selected from the group consisting of  $-\text{C(O)-}$  and  $-\text{NHC(O)-}$ ;

$\text{P}^3$  is a tertiary pharmacophore selected from the group consisting of  $\text{C}_2\text{-C}_6$  alkynyl,  $\text{C}_1\text{-C}_6$  haloalkyl, aryl, heteroaryl,  $-\text{C(O)NHR}^2$ ,  $-\text{C(O)NHS(O)}_2\text{R}^2$ ,  $-\text{NHS(O)}_2\text{R}^2$ ,  $-\text{C(O)OR}^2$  and carboxylic acid analogs, wherein  $\text{R}^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $\text{C}_1\text{-C}_4$  alkyl, substituted or unsubstituted  $\text{C}_3\text{-C}_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $\text{C}_1\text{-C}_4$  alkyl;

the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and the subscript  $q$  is 0 to 3;

$\text{L}^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $\text{C}_2\text{-C}_6$  alkylene, substituted and unsubstituted  $\text{C}_3\text{-C}_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$\text{L}^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $\text{C}_2\text{-C}_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

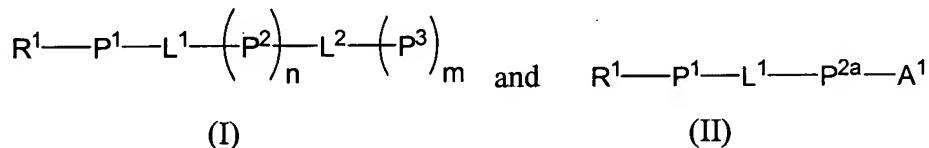
$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**37. (Withdrawn)** The method in accordance with claim 36 wherein the subject is (a) a person with diabetes mellitus whose blood pressure is 130/85 or less, (b) a person with metabolic syndrome whose blood pressure is 130/85 or less, (c) a person with a triglyceride level over 215 mg/dL, or (d) a person with a cholesterol level over 200 mg/dL.

**38. (Withdrawn)** A method for inhibiting progression of nephropathy in a subject, said method comprising administering to said subject an effective amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

**39. (Withdrawn)** The method in accordance with claim 38 wherein the subject is (a) a person with diabetes mellitus whose blood pressure is 130/85 or less, (b) a person with metabolic syndrome whose blood pressure is 130/85 or less, (c) a person with a triglyceride level over 215 mg/dL, or (d) a person with a cholesterol level over 200 mg/dL.

**40. (Withdrawn)** A method for reducing blood pressure in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5-C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-O(CH_2CH_2O)_q-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;  
 $P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)R^2$ ,  $-NHS(O)R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;  
the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and  
the subscript  $q$  is 0 to 3;  
 $L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted and unsubstituted  $C_3-C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;  
 $L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2-C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof;  
and  
 $A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**41.** (Withdrawn) The method in accordance with claim 40, said method further comprising administering to said subject an effective amount of a cis-epoxyeicosantrienoic acid.

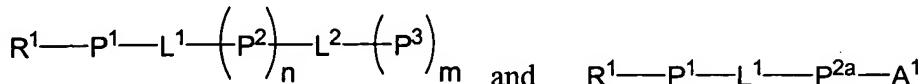
**42.** (Withdrawn) The method in accordance with claim 41, wherein said cis-epoxyeicosantrienoic acid is administered with said compound having formula (I) or (II).

**43.** (Withdrawn) A method for reducing blood pressure in a subject, said method comprising administering to said subject an effective amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

**44.** (Withdrawn) The method in accordance with claim 43, said method further comprising administering to said subject an effective amount of a cis-epoxyeicosantrienoic acid.

**45.** (Withdrawn) The method in accordance with claim 44, wherein said cis-epoxyeicosantrienoic acid is administered with said compound having formula (I) or (II).

46. (Withdrawn) A method of inhibiting the proliferation of vascular smooth muscle cells in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



(I)

(II)

and their pharmaceutically acceptable salts, wherein

$R^1$  is a member selected from the group consisting of  $C_5-C_{12}$  cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

$P^1$  is a primary pharmacophore selected from the group consisting of  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-CH_2C(O)NH-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^2$  is a secondary pharmacophore selected from the group consisting of  $-C(O)-$ ,  $-CH(OH)-$ ,  $-O(CH_2CH_2O)_q-$ ,  $-C(O)O-$ ,  $-OC(O)-$ ,  $-NHC(O)NH-$ ,  $-OC(O)NH-$ ,  $-NHC(O)O-$ ,  $-C(O)NH-$  and  $-NHC(O)-$ ;

$P^{2a}$  is selected from the group consisting of  $-C(O)-$  and  $-NHC(O)-$ ;

$P^3$  is a tertiary pharmacophore selected from the group consisting of  $C_2-C_6$  alkynyl,  $C_1-C_6$  haloalkyl, aryl, heteroaryl,  $-C(O)NHR^2$ ,  $-C(O)NHS(O)_2R^2$ ,  $-NHS(O)_2R^2$ ,  $-C(O)OR^2$  and carboxylic acid analogs, wherein  $R^2$  is a member selected from the group consisting of hydrogen, substituted or unsubstituted  $C_1-C_4$  alkyl, substituted or unsubstituted  $C_3-C_8$  cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl  $C_1-C_4$  alkyl;

the subscripts  $n$  and  $m$  are each independently 0 or 1, and at least one of  $n$  or  $m$  is 1, and the subscript  $q$  is 0 to 3;

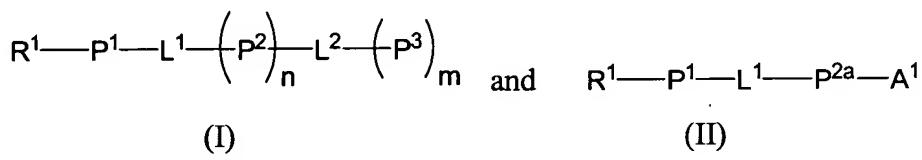
$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2-C_6$  alkylene, substituted and unsubstituted  $C_3-C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2-C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

A<sup>1</sup> is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

47. (Withdrawn) A method of inhibiting the proliferation of vascular smooth muscle cells in a subject, said method comprising administering to said subject an effective amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

48. (Withdrawn) A method of inhibiting the progression of obstructive pulmonary disease, an interstitial lung disease, or asthma in a subject, said method comprising administering to said subject an effective amount of a compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

R<sup>1</sup> is a member selected from the group consisting of C<sub>5</sub>-C<sub>12</sub> cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

P<sup>1</sup> is a primary pharmacophore selected from the group consisting of -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -CH<sub>2</sub>C(O)NH-, -C(O)NH- and -NHC(O)-;

P<sup>2</sup> is a secondary pharmacophore selected from the group consisting of -C(O)-, -CH(OH)-, -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>-, -C(O)O-, -OC(O)-, -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -C(O)NH- and -NHC(O)-;

P<sup>2a</sup> is selected from the group consisting of -C(O)- and -NHC(O)-;

P<sup>3</sup> is a tertiary pharmacophore selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, -C(O)NHR<sup>2</sup>, -C(O)NHS(O)<sub>2</sub>R<sup>2</sup>, -NHS(O)<sub>2</sub>R<sup>2</sup>, -C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl;

the subscripts n and m are each independently 0 or 1, and at least one of n or m is 1, and the subscript q is 0 to 3;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_6$  alkylene, substituted and unsubstituted  $C_3$ - $C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**49.** (Withdrawn) The method in accordance with claim 48, wherein said obstructive pulmonary disease is selected from the group consisting of chronic obstructive pulmonary disease, emphysema, and chronic bronchitis.

**50.** (Withdrawn) The method in accordance with claim 48, wherein said interstitial lung disease is idiopathic pulmonary fibrosis or is one associated with exposure to dust.

**51.** (Withdrawn) The method in accordance with claim 48, said method further comprising administering to said subject an effective amount of a cis-epoxyeicosantrienoic acid.

**52.** (Withdrawn) The method in accordance with claim 51, wherein said cis-epoxyeicosantrienoic acid is administered with said compound having formula (I) or (II).

**53.** (Withdrawn) A method of inhibiting the progression of obstructive pulmonary disease, an interstitial lung disease, or asthma in a subject, said method comprising administering to said subject an effective amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

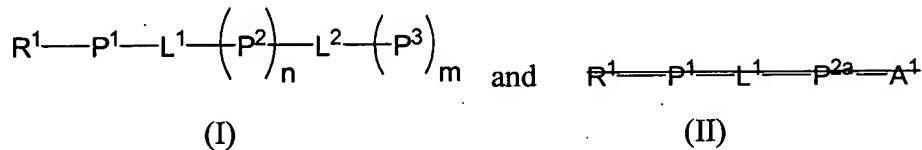
**54.** (Withdrawn) The method in accordance with claim 53, wherein said obstructive pulmonary disease is selected from the group consisting of chronic obstructive pulmonary disease, emphysema, and chronic bronchitis.

55. (Withdrawn) The method in accordance with claim 53, wherein said interstitial lung disease is idiopathic pulmonary fibrosis or is one associated with exposure to dust.

56. (Withdrawn) The method in accordance with claim 53, said method further comprising administering to said subject an effective amount of a cis-epoxyeicosantrienoic acid.

57. (Withdrawn) The method in accordance with claim 56, wherein said cis-epoxyeicosantrienoic acid is administered with said compound having formula (I) or (II).

58. (Currently Amended) A compound having a formula selected from the group consisting of:



and their pharmaceutically acceptable salts, wherein

R<sup>1</sup> is a member selected from the group consisting of C<sub>5</sub>-C<sub>12</sub> cycloalkyl[[,]]grouparyl, heteroaryl and combinations thereof, wherein said cycloalkyl portion[[s]] [[are]] is monocyclic or polycyclic;

P<sup>1</sup> is a primary pharmacophore selected from the group consisting of -NHC(O)NH-, -OC(O)NH-, NHC(O)O-, CH<sub>2</sub>C(O)NH-, C(O)NH and NHC(O)-;

P<sup>2</sup> is a secondary pharmacophore selected from the group consisting of -C(O)-, -CH(OH)-, -C(O)O-, -OC(O)-, -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -C(O)NH- [[and]] -NHC(O)- and -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>;

P<sup>2a</sup> is selected from the group consisting of C(O) and NHC(O);

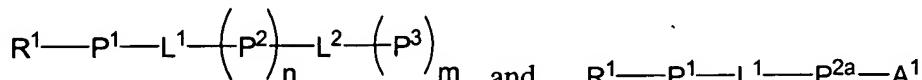
P<sup>3</sup> is a tertiary pharmacophore selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, -C(O)NHR<sup>2</sup>, -C(O)NHS(O)<sub>2</sub>R<sup>2</sup>, -NHS(O)<sub>2</sub>R<sup>2</sup>, -C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl;

the subscripts n and m are each independently 0 or 1, [[and]] at least one of n or m is 1  
and q is 0 to 3;

L<sup>1</sup> is a first linker selected from the group consisting of substituted and or unsubstituted C<sub>2</sub>-C<sub>6</sub> alkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

L<sup>2</sup> is a second linker selected from the group consisting of substituted and or unsubstituted C<sub>2</sub>-C<sub>12</sub> alkylene, substituted and unsubstituted arylene, and combinations thereof, and A<sup>1</sup> is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

59. (Original) A compound having a formula selected from the group consisting of:



(I)

(II)

and their pharmaceutically acceptable salts, wherein

R<sup>1</sup> is a member selected from the group consisting of C<sub>5</sub>-C<sub>12</sub> cycloalkyl, aryl, heteroaryl and combinations thereof, wherein said cycloalkyl portions are monocyclic or polycyclic;

P<sup>1</sup> is a primary pharmacophore selected from the group consisting of -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -CH<sub>2</sub>C(O)NH-, -C(O)NH- and -NHC(O)-;

P<sup>2</sup> is a secondary pharmacophore selected from the group consisting of -C(O)-, -CH(OH)-, -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>-, -C(O)O-, -OC(O)-, -NHC(O)NH-, -OC(O)NH-, -NHC(O)O-, -C(O)NH- and -NHC(O)-;

P<sup>2a</sup> is selected from the group consisting of -C(O)- and -NHC(O)-;

P<sup>3</sup> is a tertiary pharmacophore selected from the group consisting of C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, -C(O)NHR<sup>2</sup>, -C(O)NHS(O)<sub>2</sub>R<sup>2</sup>, -NHS(O)<sub>2</sub>R<sup>2</sup>, -C(O)OR<sup>2</sup> and carboxylic acid analogs, wherein R<sup>2</sup> is a member selected from the group consisting of hydrogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>8</sub> cycloalkyl, substituted or unsubstituted aryl and substituted or unsubstituted aryl C<sub>1</sub>-C<sub>4</sub> alkyl;

the subscripts n and m are each independently 0 or 1, and at least one of n or m is 1, and the subscript q is 0 to 3;

$L^1$  is a first linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_6$  alkylene, substituted and unsubstituted  $C_3$ - $C_6$  cycloalkylene, substituted or unsubstituted arylene and substituted or unsubstituted heteroarylene;

$L^2$  is a second linker selected from the group consisting of substituted and unsubstituted  $C_2$ - $C_{12}$  alkylene, substituted and unsubstituted arylene, and combinations thereof; and

$A^1$  is a member selected from the group consisting of an amino acid, a dipeptide and a dipeptide analog.

**60. (Currently Amended)** The compound in accordance with claim 58, wherein  $R^1$  is selected from the group consisting of  $C_5$ - $C_{12}$  cycloalkyl, phenyl and naphthyl, said cycloalkyl portion is monocyclic.

**61. - 69. (Cancelled)**

**70. (Withdrawn)** A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of claim 58.

**71. (Withdrawn)** A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of claim 59.

**72. (Withdrawn)** A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of claim 69.

**73. (Withdrawn)** A method for stabilizing biologically active epoxides in the presence of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 58 sufficient to inhibit the activity of said soluble epoxide hydrolase and stabilize said biologically active epoxide.

**74. (Withdrawn)** A method for stabilizing biologically active epoxides in the presence of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 59, sufficient to inhibit the activity of said soluble epoxide hydrolase and stabilize said biologically active epoxide.

75. (Withdrawn) A method for stabilizing biologically active epoxides in the presence of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

76. (Withdrawn) The method in accordance with claim 73, wherein said contacting is conducted in an *in vitro* assay.

77. (Withdrawn) The method in accordance with claim 73, wherein said contacting is conducted *in vivo*.

78. (Withdrawn) The method in accordance with claim 74, wherein said contacting is conducted in an *in vitro* assay.

79. (Withdrawn) The method in accordance with claim 74, wherein said contacting is conducted *in vivo*.

80. (Withdrawn) The method in accordance with claim 75, wherein said contacting is conducted in an *in vitro* assay.

81. (Withdrawn) The method in accordance with claim 75, wherein said contacting is conducted *in vivo*.

82. (Withdrawn) The method for reducing the formation of a biologically active diol produced by the action of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 58, sufficient to inhibit the activity of said soluble epoxide hydrolase and reduce the formation of said biologically active diol.

83. (Withdrawn) The method for reducing the formation of a biologically active diol produced by the action of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 59, sufficient to inhibit the activity of said soluble epoxide hydrolase and reduce the formation of said biologically active diol.

84. (Withdrawn) A method for reducing the formation of a biologically active diol produced by the action of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

85. (Withdrawn) The method in accordance with claim 82, wherein said contacting is conducted in an *in vitro* assay.

86. (Withdrawn) The method in accordance with claim 82, wherein said contacting is conducted *in vivo*.

87. (Withdrawn) The method in accordance with claim 83, wherein said contacting is conducted in an *in vitro* assay.

88. (Withdrawn) The method in accordance with claim 83, wherein said contacting is conducted *in vivo*.

89. (Withdrawn) The method in accordance with claim 84, wherein said contacting is conducted in an *in vitro* assay

90. (Withdrawn) The method in accordance with claim 84, wherein said contacting is conducted *in vivo*

91. (Withdrawn) A method for monitoring the activity of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 58 sufficient to produce a detectable change in fluorescence of said soluble epoxide hydrolase by interacting with one or more tryptophan residues present in the catalytic site of said sEH.

92. (Withdrawn) A method for monitoring the activity of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound of claim 59 sufficient to produce a detectable change in fluorescence of said soluble epoxide

hydrolase by interacting with one or more tryptophan residues present in the catalytic site of said sEH.

**93.** (Withdrawn) A method for monitoring the activity of a soluble epoxide hydrolase, said method comprising contacting said soluble epoxide hydrolase with an amount of a compound having the formula described in Tables 1-18 and their pharmaceutically acceptable salts.

**94.** (Withdrawn) The method in accordance with claim 92, wherein said compound has an aryl group present one or more components selected from the group consisting of R<sup>1</sup>, L<sup>2</sup>, P<sup>3</sup> and A<sup>1</sup>.

**95.** (New) The compound in accordance with claim 58, wherein said cycloalkyl portion is polycyclic.

**96.** (New) The compound in accordance with claim 58, wherein P<sup>2</sup> is --O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>--.

**97.** (New) The compound in accordance with claim 60, wherein P<sup>2</sup> is --O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>--.

**98.** (New) The compound in accordance with claims 95, wherein P<sup>2</sup> is --O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>--.

**99.** (New) The compound in accordance with any one of claims 96 to 98, wherein q is 0.

**100.** (New) The compound in accordance with claim 58, wherein P<sup>2</sup> is selected from the group consisting of --C(O)--, --C(O)O-- and --OC(O)--.

**101.** (New) The compound in accordance with claim 58, wherein P<sup>2</sup> is selected from the group consisting of --NHC(O)NH--, --OC(O)NH--, --NHC(O)O--, --C(O)NH--, and --NHC(O)--.

**102.** (New) The compound in accordance with claim 58, wherein P<sup>3</sup> is C<sub>2</sub>-C<sub>6</sub> alkynyl, aryl, or heteroaryl.

**103.** (New) The compound in accordance with claim 60, wherein P<sup>3</sup> is C<sub>2</sub>-C<sub>6</sub> alkynyl, aryl, or heteroaryl.

**104. (New)** The compound in accordance with claim 95, wherein P<sup>3</sup> is C<sub>2</sub>–C<sub>6</sub> alkynyl, aryl, or heteroaryl.

**105. (New)** The compound in accordance with any one of claims 58, 60 and 95 to 98, wherein P<sup>3</sup> is –C(O)OR<sup>2</sup> and a carboxylic acid analog, wherein R<sup>2</sup> is hydrogen, substituted or unsubstituted C<sub>1</sub>–C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>–C<sub>8</sub> cycloalkyl.